Project Title:	Long-Term Stability Studies of Liquid Samples from Clandestine Methamphetamine Laboratories
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Final Report:	February 1, 2006- April 30, 2007

Abstract

Solution stability data were collected from liquid samples from various stages of methamphetamine production using the Iodine/Red phosphorus reaction scheme. Solution aliquots were stored at four distinct storage conditions: *Refrigerated* (5ºC), *Ambient, Controlled Room Temperature* (25ºC/60% RH), and *Elevated Room Temperature* (40ºC). Sample solutions were pulled at defined time-points through twelve (12) months and analyzed by gas chromatography – mass spectrometry (GC-MS) to determine concentration trends of ephedrine, pseudoephedrine, and methamphetamine. The collected data was used to evaluate the precursor and final product stability based on specific sample storage conditions coupled with length of storage.

Project Description

Solution stability data will be collected for liquid samples from various stages of methamphetamine production using the Iodine/Red phosphorus reaction scheme. Solution aliquots will be stored at four distinct storage conditions: *Refrigerated* (5ºC), *Ambient, Controlled Room Temperature* (25ºC/60% RH), and *Elevated Room Temperature* (40ºC). Sample solutions will be pulled at defined time-points up to twelve (12) months and analyzed by gas chromatography – mass spectrometry (GC-MS) to determine concentration trends of ephedrine, pseudoephedrine, and methamphetamine. Results of the analyses will be used to evaluate the precursor and final product stability based on specific sample storage conditions coupled with length of storage.

Results of the analyses will be used to evaluate whether the original levels of precursors and methamphetamine remain stable based on specific sample storage conditions coupled with storage time. Actual temperature/humidity trends of several forensic laboratory evidence lockers will be collected using continuous temperature/humidity circular chart recorders for up to twelve (12) months.

Project Objectives

1. Determine if precursor only solutions convert to methamphetamine during long-term storage
2. Determine if the methamphetamine content in reaction solutions changes over time
3. Determine the advantage, if any, of refrigerated storage verses ambient storage
4. Obtain actual temperature/humidity conditions of evidence storage facilities in several forensic laboratories

Procedures

Reagents and Chemicals

- Pseudoephedrine hydrochloride (analytical standard)
- Pseudoephedrine hydrochloride tablets
- Pseudoephedrine hydrochloride liquid capsules (gel tabs)
- Ephedrine hydrochloride (analytical standard)
- Sodium chloride
- Sodium hydroxide (pellets)
- Iodine (beads)
- Diethyl ether
- Hexane
- Chloroform
- Red phosphorus (powder)
- Sulfuric acid (concentrated)
- Methanol
- Sodium sulfate
- Hydrochloric acid

Equipment and Instrumentation

- Reflux apparatus equipped with a heating mantle, a 1000-mL round-bottom flask, and a reflux condenser
- Eppendorf adjustable pipette, 500 – 2500 μL
- Dickson circular temperature chart recorders
- Dickson Temperature/Humidity circular chart recorders
- Hewlett-Packard/Agilent Gas Chromatograph/Mass Selective Detector system (HP6890 series/5973 MSD) coupled with a data system
- Fisher Scientific IsoTemp Model 525D refrigerator for 5ºC storage
- Fischer Scientific IsoTemp Model 650G oven with variable temperature setting for 40ºC sample storage
- Hotpack 10-ft^3 bench-top stability chamber for 25ºC/60% RH storage
- Mettler analytical balance
- Two SafeAire four-foot fume hoods and one Labconco six-foot fume hood.

Samples

Sixteen separate solutions were prepared in an effort to properly monitor the stability of precursor solutions as well as solutions taken from various points of the synthetic route. The specific solutions are listed below:

- Pure pseudoephedrine hydrochloride in deionized water
- Pure pseudoephedrine hydrochloride in methanol
- Pure ephedrine hydrochloride in deionized water
- Pure ephedrine hydrochloride in methanol
- Pseudoephedrine tablets in deionized water
- Pseudoephedrine tablets in methanol
- Pseudoephedrine liquid capsules in aqueous (high pH)
- Pseudoephedrine liquid capsules in aqueous (high pH) and Diethyl ether
- Pure pseudoephedrine hydrochloride, iodine, and red phosphorus in deionized water
- Pure ephedrine hydrochloride, iodine, and red phosphorus in deionized water
- Methamphetamine and reaction by-products (unfiltered) in aqueous (low pH)
- Methamphetamine and reaction by-products (filtered) in aqueous (low pH)
- Methamphetamine and reaction by-products (filtered) in aqueous (high pH)
- Methamphetamine and reaction by-products (filtered) in aqueous (high pH) and diethyl ether
- Methamphetamine free-base in diethyl ether
- Methamphetamine hydrochloride in diethyl ether

Preparation of solutions

Pure ephedrine hydrochloride and pseudoephedrine hydrochloride solutions

Pseudoephedrine hydrochloride (pure) in deionized water: A 2.01 grams portion of pure pseudoephedrine hydrochloride was added to 200 mL of deionized water.

Pseudoephedrine hydrochloride (pure) in methanol: A 2.01 grams portion of pure pseudoephedrine hydrochloride was added to 200 mL of methanol.

Ephedrine hydrochloride (pure) in deionized water: A 2.00 grams portion of pure ephedrine hydrochloride was added to 200 mL of deionized water.

Ephedrine hydrochloride (pure) in methanol: A 2.00 grams portion of pure ephedrine hydrochloride was added to 100 mL of methanol.

Pseudoephedrine tablet and liquid capsule solutions

Pseudoephedrine tablets in deionized water: Forty-eight pseudoephedrine tablets containing 30 mg each were ground up and dissolved in 200 mL of deionized water.

Pseudoephedrine tablets in methanol: Forty-eight pseudoephedrine tablets containing 30 mg each were ground up and dissolved in 200 mL of methanol.

Pseudoephedrine liquid capsules in aqueous solution, high pH: Forty-eight pseudoephedrine liquid capsules containing 30 mg each were cut open and dissolved in 50 mL of hot water for approximately five minutes with stirring followed by the addition of 50 mL of methanol. The solution was allowed to sit so the insolubles could settle out after which 100 mL was removed and added to 100 mL of a 10% NaOH solution.

Pseudoephedrine liquid capsules in aqueous solution, high pH, and Diethyl ether: Forty-eight pseudoephedrine liquid capsules containing 30 mg each were cut open and dissolved in 50 mL of hot water for approximately five minutes with stirring followed by the addition of 50 mL of methanol. The solution was allowed to sit so the insolubles could settle out after which 100 mL was removed and added to 100 mL of a 10% NaOH solution. A 100 mL portion of diethyl ether was added and mix vigorously.

Pure pseudoephedrine hydrochloride, iodine, and red phosphorus

With constant stirring, to a 100-mL portion of deionized water was added 50.15 grams of pure pseudoephedrine hydrochloride, 15.15 grams of red phosphorus, and 102.90 grams of iodine beads.

Pure ephedrine hydrochloride, iodine, and red phosphorus

With constant stirring, to a 100-mL portion of deionized water was added 50.14 grams of pure ephedrine hydrochloride, 15.15 grams of red phosphorus, and 100.08 grams of iodine beads.

All remaining solutions

Refer to the synthesis procedure for preparation of all remaining solutions.

Synthesis of Methamphetamine

A reflux system was set up with a 1000-mL round bottom flask containing glass boiling beads, a reflux condenser, and a heating mantle. A constant supply of cold water ran through the condenser. The reflux system was supported by a ring stand and was set up inside a properly working fume hood.

The following chemicals were added to the 100-mL round bottom flask: 167.01 grams of pure pseudoephedrine hydrochloride, 50.39 grams of red phosphorus and 250 mL of deionized water. The solution was gently swirled for complete dissolution followed by *slowly* adding 300.14 grams of iodine beads. The solution was heated via the heating mantle to boiling and allowed to reflux for one hour with constant monitoring.

At the conclusion of refluxing, the solution was allowed to cool to room temperature[1]. Following a dilution with approximately 200 mL of deionized water, the solution was filtered through numerous coffee filters to remove the red phosphorus and other insolubles[2]. The solution was then transferred to a 1000 mL beaker and placed on a magnetic stirrer. With stirring, the solution was made strongly basic (pH > 10) with 250-300 mL of a saturated sodium hydroxide solution[3]. The basified solution was washed with diethyl ether to extract out the methamphetamine free base[4] (100 mL aliquots of the basified solution washed two times with 100 mL aliquots of diethyl ether and repeated four times).

All of the diethyl ether portions were then combined in a beaker[5]. An HCl gas generator was created using rubber tubing, a glass pipette, a rubber stopper, and a 500-mL Erlenmeyer flask. A 25 gram portion of sodium chloride and a 100 mL portion of concentrated sulfuric acid were added to the generator. Using the tubing, the resultant HCl gas was fumed through the diethyl ether until no more methamphetamine hydrochloride precipitated out[6].

Time-point Analysis

A schedule of analyses was prepared to monitor the stability of solutions over the course of twelve months. The schedule included the specific pull dates, the number of samples analyzed at each time-point, the temperature conditions examined at each time point, and the specific analyses performed at each time point. An example of the schedule is depicted in the following figure.

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[1] A 100 mL aliquot of the "Methamphetamine, residual reaction products (*unfiltered*) in *low* pH aqueous" solution was collected at this point.
[2] A 100 mL aliquot of the "Methamphetamine, residual reaction products (*filtered*) in *low* pH aqueous" solution was collected at this point.
[3] A 100 mL aliquot of the "Methamphetamine, residual reaction products (*filtered*) in *high* pH aqueous" solution was collected at this point.
[4] A 100 mL aliquot of the "Methamphetamine, residual reaction products (filtered) in high pH aqueous and diethyl ether" solution was collected at this point. Portions of each layer after the washing were collected.
[5] A 100 mL aliquot of the "Methamphetamine free base in diethyl ether" solution was collected at this point.
[6] A 100 mL aliquot of the "Methamphetamine HCl in diethyl ether" solution was collected at this point. The aliquot contained both liquid and precipitate.

Evaluation Intervals and Conditions:

	Time (Month)								
Stability Conditions	0	½	1	2	3	6	9	12	# of samples stored
Initial*	2A,P								1
5°C		3A,P	3A,P	3A,P	3A,P	3A,P	3A,P	3A,P	1
Ambient		3A,P	3A,P	3A,P	3A,P	3A,P	3A,P	3A,P	1
25°C/60% RH		3A,P	3A,P	3A,P	3A,P	3A,P	3A,P	3A,P	1
40°C/75% RH		3A,P	3A,P	3A,P	X	X	X	X	1
Pull Dates**									
Notebook Ref.									

Testing Requirements:

* Initial analyses to be performed on 3 separate days.
** ± 5 working days

A = GC/MS assay, Impurity profile by GC/MS
P = Appearance (visual)
X= No testing performed
Numeral = Number of units tested at each interval and storage condition.

Stability Chambers

After the initial three-day testing period, all solutions were dispersed into four separate stability chambers designated as: *Refrigerated* (5ºC), *Ambient, Controlled Room Temperature* (25ºC/60% RH), and *Elevated Room Temperature* (40ºC).

Sample analysis

The following analyses were performed on each sample during each time-point.

Appearance Testing

All samples were examined visually for their general appearance. Colors, precipitates, multiple layers, and other visual characteristics were noted, if present, and documented. Changes in visual appearance are often good indicators of changes in the sample composition.

Extraction

All solutions, regardless of pH, underwent a basic extraction. In general, an aliquot of each sample was basified using 0.1 N NaOH and then extracted into chloroform. Variations of this general procedure depended on the chemical composition of the solution and the anticipated concentration of methamphetamine and/or precursor. Regardless, all aqueous solution aliquots and chloroform extraction volumes remained constant throughout the study.

GC/MS Analysis

Samples underwent GC/MS analysis using the following parameters:

Method name: Tempro.m

Instrument conditions:
Oven temperature program:
Initial temperature – 85ºC
Rate 1 – 20ºC/minute to 260ºC, hold 2.00 minutes
Rate 2 – 30ºC/minute to 310ºC, hold for 0.50 minute
Total run time – 12.92 minutes
Mass range – 40 to 400 a.m.u.
Split ratio – 50:1
Injector temperature – 250ºC
Interface temperature – 280ºC

Evidence Storage Facility Monitoring

The sponsoring laboratory and five additional forensic laboratories kept a temperature/humidity circular chart recorder in their respective evidence storage facility for the entire duration of the twelve month study. These recorders documented the actual temperature/humidity conditions of the evidence storage facility over the course of a year. Each lab was responsible for changing out the circular charts at a specified time each week and forwarding those charts to the Principle Investigator on a monthly basis.

The participating laboratories were:

- Johnson County (Kansas) Sheriff's Office
- Kansas Bureau of Investigation
- Kansas City (Missouri) Police Department
- Missouri State Highway Patrol
- Wisconsin State Crime Laboratory
- Western Forensic Law Enforcement Training Center

Results/Discussion

Determine if precursor only solutions convert to methamphetamine during long-term storage

No spontaneous conversion from pseudoephedrine or ephedrine into methamphetamine was detected regardless of sample composition (pure standard, tablet, or liquid capsule), solvent (water or methanol), or storage condition. The impact of these findings is that pseudoephedrine and ephedrine will only convert into

methamphetamine when they are place in chemical environments intended to bring about such a conversion.

Although no spontaneous conversion was detected, some sample degradation did occur with specific solutions. This sample degradation has a direct impact on potential quantitative analyses performed after collection. The specific degradation detected is briefly discussed below.

When methanol solutions containing pure ephedrine chloride were stored at 5ºC, suspended white crystals began appearing at the Month Two time-point. Extraneous peaks were also observed during GC/MS analysis at the same time. No similar observations were made with ephedrine stored at other conditions or in deionized water. While none of the extraneous peaks were identified the presence of the crystals and peaks indicates a loss of ephedrine content over time.

As a recommendation, if quantitation is necessary, ephedrine in methanol solutions stored at 5ºC should be analyzed within one month to reduce the possibility of decreased calculations.

Solutions from the extraction of pseudoephedrine liquid capsules began to contain increasing amounts of three different oxazolidines. Pseudoephedrine spontaneously condenses into an oxazolidine in the presence of aldehydes or ketones. The formation of oxazolidines occurred in all solutions of pseudoephedrine liquid capules regardless of the storage temperature. However, the formation was less dramatic at 5ºC but substantially higher in the presence of diethyl ether. The first solid indication of oxazolidines occurred at the Month Two time-point. In certain solutions, namely *Pseudoephedrine liquid capsules in aqueous (high pH) and Diethyl ether* stored at 25ºC/60% RH, the peak areas of the oxazolidines became greater than the peak area of the pseudoephedrine at the end of the stability study. This represents a substantial decrease in pseudoephedrine content in these solutions.

As a recommendation, if quantitation is necessary, all solutions of pseudoephedrine extracted from liquid capsules should be stored at 5ºC and analyzed within one month. Analysis beyond one month may result in lower calculations based on the conversion of pseudoephedrine into its oxazolidines.

Determine if the methamphetamine content in reaction solutions changes over time

For solutions which originally contained methamphetamine (all post-reaction solutions), no definitive change of methamphetamine content was observed. Any potential changes were very minor and less than the ±5% which most labs use as an understood degree of uncertainty.

One solution type *did* undergo a change in methamphetamine content over the course of the stability study. This solution was pure pseudoephedrine hydrochloride, iodine, and red phosphorus in deionized water. This solution did not contained any

methamphetamine when prepared. However, over the course of the study, the presence of methamphetamine at all stability conditions, although at very minute levels, was apparent. In fact, at 40ºC, there was clear conversion of some pseudoephedrine into methamphetamine after two months.

One would expect the same results if the pseudoephedrine was replaced with ephedrine. However, this was not the case. Solutions of ephedrine hydrochloride, iodine, and red phosphorus in deionized water did not contain detectable levels of methamphetamine after twelve months when stored at 5ºC, *Ambient*, or 25ºC/60% RH conditions. However, like pseudoephedrine, there was clear conversion of some ephedrine into methamphetamine after two months when stored at 40ºC.

Although the content of methamphetamine did not appear to change substantially for solutions stored at 5ºC, *Ambient*, or 25ºC/60% RH conditions, physical appearance of some solutions did change. Of note, many solutions which started out yellow or very light brown gradually changed to a distinct brown color over time. As mentioned above, changes in physical appearance often indicate future changes in content.

As a recommendation, if quantitation is necessary, solutions containing methamphetamine should be stored at 5ºC and analyzed within one month.

Determine the advantage, if any, of refrigerated storage verses ambient storage

Samples stored at 5ºC had less change in their solution composition over time than identical samples stored at *Ambient* or 25ºC/60% RH conditions. As discussed above, ephedrine hydrochloride in methanol is an exception. As a recommendation, all solutions from methamphetamine labs should be stored at refrigerated conditions while at the laboratory, *especially* if quantitation of any form is anticipated.

Obtain actual temperature/humidity conditions of evidence storage facilities in several forensic laboratories

Over the course of twelve months, the temperature conditions of the monitored evidence storage facilities fluctuated, on average, less than ±10ºF. Most of the time, the temperature remained within ±5ºF around an average value. The average, annual temperature for each laboratory is given below:

- Johnson County Sheriff's Office
  70.6ºF (21.4ºC)
- Kansas City Police Department
  73.4ºF (23.0ºC)
- Missouri State Highway Patrol
  62.0ºF (16.7ºC)
- Wisconsin State Police
  63.7ºF (17.6ºC)

- Kansas Bureau of Investigation
  70.0ºF (21.1ºC)
- Western Forensic Law Enforcement Training Center
  68.7ºF (20.4ºC)

As seen in the above data, all temperatures consistently remained below the 25ºC defined as *Controlled Room Temperature*, even during the heat of the summer.

As a general rule, if storage at 5ºC is not possible, ambient temperature conditions in *Midwest* crime laboratories will probably not cause *substantial* degradation of solutions if analyzed within a few months. However, individuals laboratories must determine if small amount of anticipate degradation expected at ambient storage is acceptable.

Final Recommendations

Based on the data obtained throughout the study, the following guidelines are recommended for analysis of solutions from clandestine methamphetamine laboratories:

- If quantitation of ephedrine/pseudoephedrine or methamphetamine is anticipated, then solutions should be stored at 5ºC and testing should occur within one month.
- If quantitation will not occur, then solutions can be stored at *Ambient* conditions and testing should occur within three months.

However, caution should be taken since none of this takes into account sample storage prior to submission to the laboratory.

Dissemination Discussion

The results of the study were presented at the 2007 Annual meeting of the *Midwest Forensic Resource Center*. Additionally, the Principal Investigator has already been accepted to present the results at the 2007 annual technical seminar of the *Clandestine Laboratory Investigating Chemists Association*.

Other plans for dissemination include submitting a presentation proposal for the 2007 annual fall meeting of the *Midwestern Association of Forensic Scientists* and publishing the results in a peer-reviewed journal, such as the *Journal of the Clandestine Laboratory Investigating Chemists Association* or the *Journal of Forensic Sciences*. The specific journal and the number of manuscripts to be prepared from the research has not been determined at this time.

Finally, Mr. Gary Bombard, retired from the Illinois State Police, has submitted an NIJ Solicitation for Training involving a blended training format for forensic scientists. The format would include web-based training and on-site training. Mr. Bombard has included

the material presented at the *Midwest Forensic Resource Center* annual meeting as part of this Solicitation. If accepted, the material would be available as a web-based training opportunity.